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Incidence of gynaecological cancer during the COVID-19 pandemic: A population-based study in the Netherlands

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ABSTRACT

Objective: To study the impact of the COVID-19 pandemic and consequent lockdown on the number of diagnoses of gynaecological malignancies in the Netherlands.
Methods: We performed a retrospective cohort study using data from the Netherlands Cancer Registry (NCR) on women of 18 years and older diagnosed with invasive endometrial, ovarian, cervical or vulvar cancer in the period 2017–2021. Analyses were stratified for age, socioeconomical status (SES) and region.
Results: The incidence rate of gynaecological cancer was 67/100.000 (n = 4832) before (2017–2019) and 68/100.000 (n = 4833) during (2020) the COVID-19 pandemic. Comparing the number of diagnoses of the two periods for the four types of cancer separately showed no significant difference. During the first wave of COVID-19 (March-June 2020), a clear decrease in number of gynaecological cancer diagnoses was visible (20–34 %). Subsequently, large increases in number of diagnoses were visible (11–29 %). No significant differences in incidence were found between different age groups, SES and regions. In 2021 an increase of 5.9 % in number of diagnoses was seen.
Conclusion: In the Netherlands, a clear drop in number of diagnoses was visible for all four types of gynaecological cancers during the first wave, with a subsequent increase in number of diagnoses in the second part of 2020 and in 2021. No differences between SES groups were found. This illustrates good organisation of and access to health care in the Netherlands.

1. Introduction

On 13 March 2020, the WHO declared Europe the epicentre of the coronavirus disease 2019 (COVID-19) pandemic. Europe has the highest number of reported cases and deaths compared to the rest of the world, except China [1]. The first COVID-19 infection in the Netherlands was confirmed in February 2020, and quickly spread throughout the country with over eight and a half million confirmed cases, over 22.000 deaths and over 36 million vaccine doses by 8 November, 2022 [2,3].

To contain the spread of COVID-19, the Dutch government implemented an 'intelligent lockdown' in March 2020 [4,5]. The second lockdown was proclaimed in October as a 'partial lockdown'. However, a full lockdown was proclaimed in December 2020 as the incidence of COVID-19 continued to rise. In January 2021, the Netherlands started to vaccinate against COVID-19 and in July 2021 the lockdown was lifted. Due to increased COVID-19 infections, a new lockdown was implemented in November 2021 [4].

Studies from several countries, including the Netherlands, demonstrated a decrease in cancer diagnosis and surgical volume during the COVID-19 pandemic [3,6–16]. However, these studies only assessed the specific impact of the pandemic on the incidence of the different types of gynaecological cancer during the first wave in 2020, not over a longer period. Since the four most common types of gynaecological cancer (endometrial, ovarian, cervical and vulvar cancer) differ greatly in terms of symptoms, risk factors and mean age of affected patients, the impact of the COVID-19 pandemic and subsequent lockdown could have had various effects on the incidence of the cancer types [17–20]. Moreover, the afore mentioned studies on the effect of the COVID-19 pandemic on cancer diagnosis did neither include the effect of different socio-economic status groups (SES-groups) on cancer diagnosis nor the

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impact of the severity of the pandemic. Patients with low SES are known to have a poorer life expectancy, and it could be hypothesised that the impact of the pandemic or the lockdown may have led to differences between SES groups [21]. Knowledge of the specific impact of the pandemic on the incidence of the different gynaecological cancers and different SES groups will allow a more detailed insight on the impact of the pandemic and could help tackle future challenges in cancer care during lockdowns and periods of extreme demands on healthcare.

In this population-based study, using reliable data from the national cancer registry (NCR), we aim to evaluate the impact of the COVID-19 pandemic on gynaecological cancer diagnosis in the Netherlands with great detail.

2. Methods

2.1. Data collection

A retrospective population-based cohort study was performed using data from the Netherlands Cancer Registry (NCR). The NCR is a population-based registry for all newly diagnosed malignancies in the Netherlands since 1989. It is based on notification by the registry for histo- and cytopathology (PALGA), Dutch hospital data (DHD) or haematology laboratories. The data is routinely extracted from medical files from Dutch hospitals by extensively trained and experienced registration clerks [22].

The current study included all patients who were diagnosed with either endometrial, ovarian, cervical and/or vulvar cancer in the period 2017–2021 in the Netherlands. All patients had an invasive tumour and were 18 years or older. Patients with synchronous primary tumours of different types were categorised as both types.

2.2. Definitions

The data was divided into two time periods: before (2017, 2018 and 2019) and during the COVID-19 pandemic (2020). The social economic status (SES) was based on the patients zip code at time of diagnosis. The SES was calculated using the median household income and the average real estate valuation (WOZ value) and categorised as low, middle or high, based on data from Statistics Netherlands [23]. SES was only analysed for the total population, endometrial cancer and ovarian cancer. The incidence of cervical and vulvar cancer was too low to conduct meaningful analyses (<10 patients/month). Age was divided into three categories (<60 years, 60–79 years, 80+ years) for the total population, endometrial cancer and ovarian cancer. For cervical and vulvar cancer only two age groups were used since the incidence was too small to conduct meaningful analyses for more groups (<10 patients/month). For cervical cancer it was divided into ≤ 60 and > 60 years, as women undergo screening until the age of 60 [24]. Vulvar cancer age was divided into ≤ 70 and > 70 years, since over half of the patients are older than 70 years [25]. Patients were divided into provinces based on the zip code of the hospital at time of diagnosis (Friesland, Groningen, Drenthe, Gelderland, Flevoland, Overijssel, Noord-Brabant, Limburg, Noord-Holland, Zuid-Holland, Utrecht, Zeeland). Per province the cumulative burden of COVID-19 was calculated per 100.000 citizens for the first wave of COVID-19 based on data of the National Institute for Public Health and the Environment and statistics Netherlands [26,27]. The COVID-19 burden was divided into three categories (0–150, 151–300, <300 per 100.000 citizens). Change in incidence was calculated per region of COVID-19 burden in the Netherlands. To assess the impact of the pandemic after the first year, we calculated the incidences and incidence rates for the four types of gynaecological cancer in 2021.

2.3. Statistical analyses

For each period, the number of new cancer diagnoses was calculated for endometrial, ovarian, cervical and vulvar cancer, as well as for all four types combined. The incidence before COVID-19 was calculated by using the mean incidence of the years 2017, 2018 and 2019. The minimum and maximum incidences were calculated for this period. To calculate the differences between before COVID-19 and 2020, the chi-square test was used. Incidence per month and per region were calculated for the period before COVID-19 and 2020. The incidence per region for the four types of cancer combined was additionally calculated for the period during the first wave (March-June). Comparisons were stratified by type of cancer, SES, age and region. No stratified analyses where performed with an incidence < 10. The incidence rate (IR) per 100.000 women was calculated for both time periods using data available from Statistics Netherlands and based on the number of women aged 18 and over inthe total population on 1 January of that year in the Netherlands [28]. The IR was not calculated for SES since the population numbers were not available per group. The difference in absolute number of diagnoses was calculated using the incidence rate. The change in incidence was calculated as the percentual difference in incidence between before COVID-19 and 2020. All analyses were performed using STATA 16.1 (StataCorp, College Station, Texas, USA). P values < 0.05 were considered statistically significant.

3. Results

The incidence rate for gynaecological cancer before the COVID-19 pandemic was 67/100.000 women (n = 4832), and the incidence rate during the pandemic was 68/100.000 women (n = 4833). There were no significant differences in the incidences before (2017–2019) and during COVID-19 (2020) for the different cancer types, SES-groups nor age-groups (Table 1).

The period during COVID-19 (2020) was analysed in more detail, showing that the incidences of all four cancer types notably decreased during the first wave of COVID-19 and corresponding lockdown compared to before COVID-19 (2017–2019, Fig. 1**A-1D**). After the first wave (July – December 2020), the incidence of all four types of cancer increased with higher incidences compared to before COVID-19.

3.1. The influence of age on the incidence of gynaecological cancer

The impact of age on the incidence of gynaecological cancer during the COVID-19 pandemic is displayed in detail in Table 1 and Fig. 2. Patients < 60 years showed a decrease (−2.1 %), while patients of 80 + years showed an increase (2.4 %) in gynaecological cancer diagnoses (Table 1). During the first wave of COVID-19, the incidence of endometrial cancer decreased in all three age groups and subsequently increased after the first wave (Fig. 2**A**). For ovarian cancer large increases in incidence were visible for the age groups <60 and 80 + years after the first wave and the incidence decreased after the second lockdown (Fig. 2**B**). For cervical cancer the largest decrease in incidence in cervical cancer patients was seen in the group ≤ 60 years (−4.7 %, Table 1). Both age groups in cervical cancer showed similar decreases in diagnoses during the first wave and increases after the first wave (Fig. 2**C**). For vulvar cancer, a decrease in incidence was only observed in patients of ≤ 70 years (−4.7 %, Table 1).

3.2. The influence of SES on the incidence

For all gynaecologic cancers together, the decrease in incidence for patients with intermediate and high SES were similar (−1.1 %, −1.9 % respectively, Table 1). In endometrial cancer, the incidence in patients with a low SES showed a decrease (−1.4 %, Table 1). The incidence in patients with low SES decreased during the second lockdown compared to before COVID-19, while the incidence in the other SES groups increased, aligning to the incidence before the pandemic (2017–2019, Fig. 3**A**). In ovarian cancer, a decrease in incidence was visible in the high SES group (−5.2 %, Table 1). Increases were visible in patients with low SES after the first wave and decreased after the second lockdown,

Table 1
Incidence of gynaecological cancer before and during COVID-19, by cancer type, age, SES and region.

		Before COVID-19 (2017-2019) N (IR)	During COVID-19 (2020) N (IR)	Difference*	p-value
All types of gynaecological cancer	**Cancer type**				NS
	Endometrial	2118 (30)	2143 (30)	1.2%	
	Ovarian	1440 (20)	1462 (21)	1.5%	
	Cervical	834 (12)	797 (11)	-4.4%	
	Vulva	440 (6)	431(6)	-2.0%	
	Age				NS
	<60	1575 (33)	1542 (32)	-2.1%	
	60-79	2517 (139)	2532 (135)	0.6%	
	80+	741 (153)	759 (150)	2.4%	
	SES				NS
	Low	1371	1377	0.4%	
	Intermediate	1626	1608	-1.1%	
	High	1322	1297	-1.9%	
	Unknown	513	551		
	Region				NS
	North	575 (82)	554 (78)	-3.7%	
	East	1010 (69)	1024 (69)	1.4%	
	South	1073 (72)	1085 (71)	1.1%	
	West	2172 (95)	2166(63)	-0.3%	
	Unknown	2	4		
Endometrial cancer	**Age**				NS
	<60	454	449	-1.1%	
	60-79	1335	1374	2.9%	
	80+	329	320	-2.7%	
	SES				NS
	Low	574	566	-1.4%	
	Intermediate	727	737	1.4%	
	High	591	608	2.9%	
	Unknown	226	232		
	Region				NS
	North	257	254	-1.2%	
	East	462	479	3.7%	
	South	471	486	3.2%	
	West	927	922	-0.5%	
	Unknown	1	2		
Ovarian cancer	**Age**				NS
	<60	399	394	-1.3%	
	60-79	803	800	-0.4%	
	80+	238	268	12.6%	
	SES				NS
	Low	379	387	2.1%	
	Intermediate	491	492	0.2%	
	High	426	404	-5.2%	
	Unknown	144	179		
	Region				NS
	North	164	150	-8.5%	
	East	307	335	9.1%	
	South	332	330	-0.6%	
	West	636	647	1.7%	
	Unknown	1	0		
Cervical cancer	**Age**				NS
	≤60	632	602	-4.7%	
	>60	202	195	-3.5%	
	SES				NS
	Low	268	268	0%	
	Intermediate	266	241	-9.4%	
	High	204	196	-3.9%	
	Unknown	96	92		
	Region				NS
	North	100	96	-4.0%	
	East	144	114	-20.8%	
	South	179	172	-3.9%	
	West	412	415	-0.7%	
	Unknown	0	0		
Vulvar cancer	**Age**				NS
	≤70	211	201	-4.7%	
	>70	229	230	0.4%	
	SES				NS
	Low	150	156	4.0%	
	Intermediate	142	138	-2.8%	
	High	101	89	-11.9%	
	Unknown	47	48		
	Region				NS

(*continued on next page*)

Table 1 (*continued*)

		Before COVID-19 (2017-2019) N (IR)	During COVID-19 (2020) N (IR)	Difference*	p-value
	North	55	54	-1.8%	
	East	98	96	-2.0%	
	South	90	97	7.8%	
	West	196	182	-7.1%	
	Unknown	1	2		

Data are reported as n of patients (incidence rate per 100.000 women) unless otherwise indicated. Significance was tested using the chi^2 **Calculated as the difference between the period before COVID-19 (2017-2019) and 2020. Abbreviation: IR incidence rate, SES socioeconomic status, NS not statistically significant*

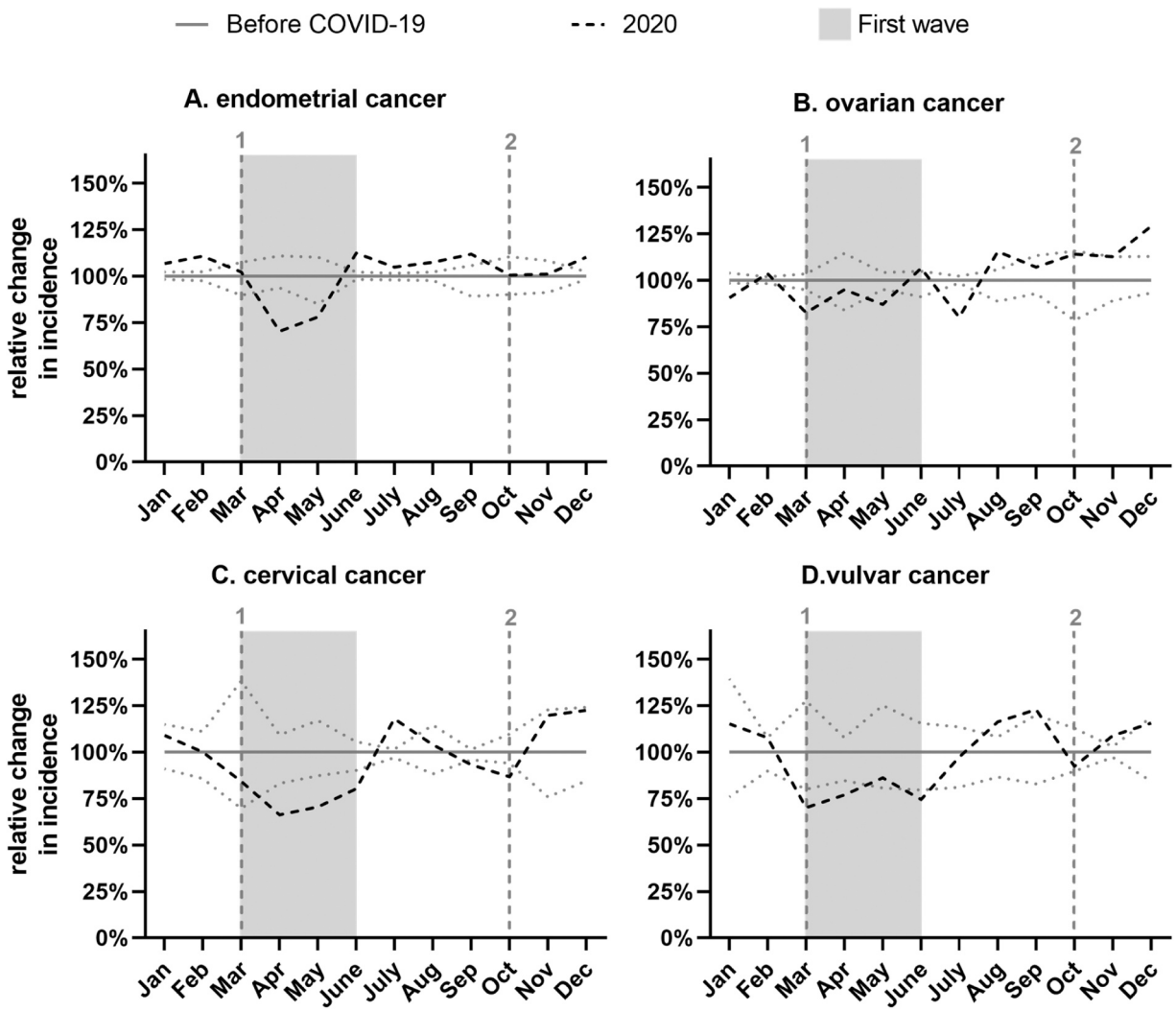

Fig. 1. Incidence of gynaecological cancers before and during COVID-19. The change in incidence for the four types of gynaecological cancers: endometrial (A), ovarian (B), cervical (C) and vulvar (D) cancer for the period before COVID-19 (2017–2019; with its minimum and maximum incidence: grey dotted line) and 2020 per month. [1]first lockdown 2020, [2]second lockdown 2020.

while the incidence increased after the lockdown for the patients with intermediate and high SES (Fig. 3**B**).

3.3. The influence of severity of the pandemic on the incidence

In the northern provinces of the Netherlands, the number of COVID-19 affected patients during the first wave was much lower than in the southern provinces, as depicted in Fig. 4. During the first wave, an increase in incidence in gynaecological cancer diagnoses was visible in the southern region with an intermediate COVID-19 burden (51–200 positive COVID-19 patients per 100.000 citizens). The largest decreases in incidence in gynaecological cancer were seen in the central and the southern parts of the Netherlands in intermediate and high COVID-19 burden regions. The area with a low COVID-19 burden showed a small decrease in number of diagnoses.

3.4. Incidence after the first year of COVID-19

In 2021 the incidence for all types of gynaecological cancer increased to 5118, with an incidence rate of 71/100.000 women. That is an increase of 5.9 % compared to the period before (2017–2019, IR 67/100.000 women) and 5.9 % during the pandemic (2020, IR 68/100.000 women). Compared to the period before the COVID-19 pandemic, the largest increase in diagnoses was visible for cervical cancer (13.7 %)

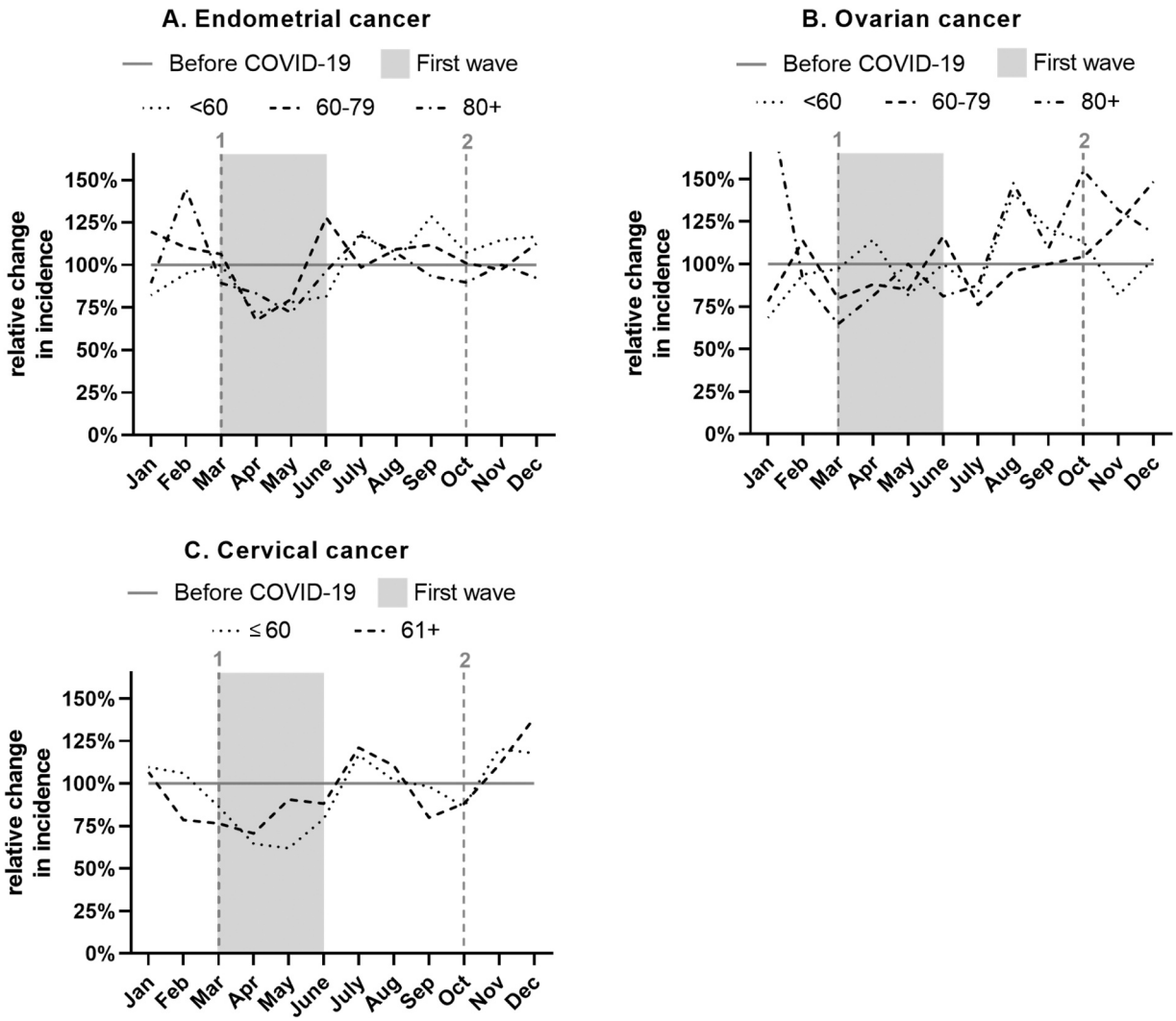

Fig. 2. Change in incidence over time for each age group. The change in incidence for three types of gynaecological cancers: endometrial (A), ovarian (B) and cervical (C) cancer for the period before COVID-19 (2017–2019) and during COVID-19 (2020) per age group per month. [1]first lockdown 2020, [2]second lockdown 2020.

followed by endometrial cancer (8.8 %) and vulvar cancer (2.7 %). A decrease was visible for ovarian cancer (−1.9 %). To assess whether the incidence was normalised after the COVID-19 pandemic, we compared the mean incidence of 2020 and 2021 together (n = 4976) with the period before COVID-19 (n = 4832) in order to display trends over time. There was an overall increase in incidence of 3.0 %.

4. Discussion

Our results showed an unequivocal decrease in the number of gynaecological malignancies during the first wave of COVID-19 and especially during the first lockdown period in the Netherlands. Furthermore, our results showed an partial catch-up in incidence in 2021, suggesting delayed diagnosis.

As presented by others, we showed a decrease in gynaecological cancer diagnoses [3,6,29]. For the four types of gynaecological cancer the study of Dinmohamed et al. showed a decrease in incidence of up to approximately 30 %, the study of Jacob et al. found a decrease in incidence of 3.9–26.4 % and Tsibulak et al. reported a decrease in incidence of 34 %−53 % [3,6,29]. Interestingly these previous studies showed larger decreases in incidences of the gynaecological cancers compared to the results we present. The differences in outcomes between the studies are likely due to the fact that we assessed a longer period: we took the whole of 2020 into account and consequently the catch-up after the first wave is included in our results. Moreover, the absolute incidences are higher in our study compared to the previous studies (before COVID-19 n = 4832, 2020 n = 4833), which increases our statistical power.

The cause of the decrease in incidence in 2020 is multifactorial. Patient delay may have been caused by both fear of contracting COVID-19 in the hospital and by concern to burden the healthcare workers with their non-COVID-19 related symptoms, and consequently delayed visits [30]. This phenomenon was seen in a Dutch study which suggested that the decline in admission rates could be partially explained by fear of the novelty of the disease, as well as by the lockdowns and the social distancing [31]. This theory is supported by our finding that the largest, although not significant, decrease in incidence was seen in the 80 + years age groups, who are considered to be the most vulnerable (and consequently most frightened) patients for COVID-19 [32]. Furthermore, symptoms of gynaecological cancer, especially ovarian cancer, are frequently unspecific, and therefore not directly associated with cancer by patients. Tsibulak et al. found that of the patients who visited the hospital in 2020, significantly more presented with tumour-specific symptoms compared to 2019. They suggested that patients with tumour-specific symptoms were forced by their symptoms to visit a doctor, while patients with non-specific symptoms (e.g. symptoms caused by ovarian cancer) delayed their visit or did not go at all [6].

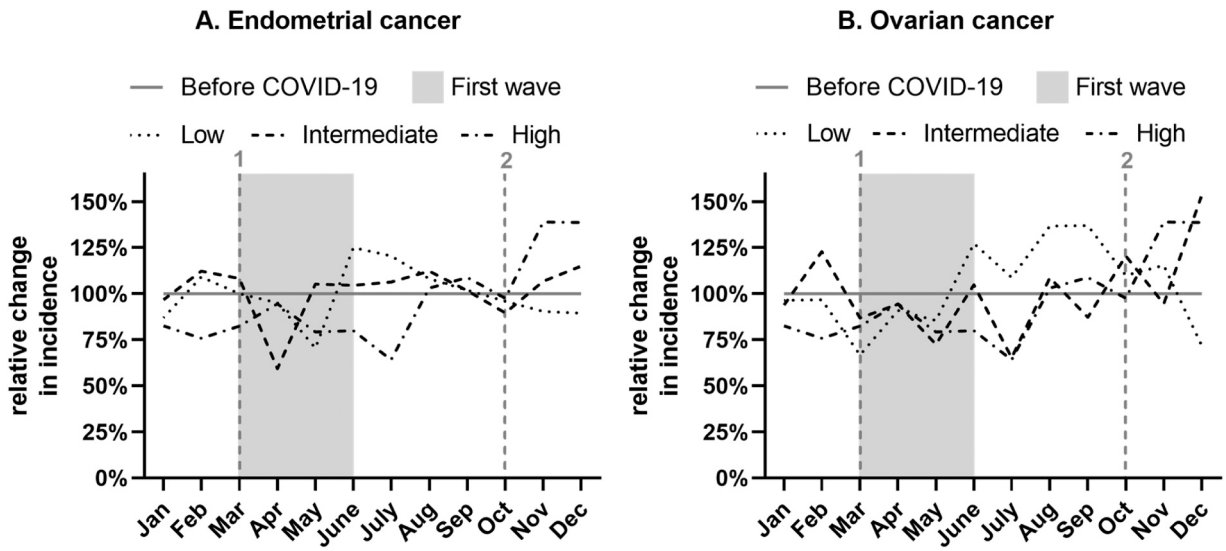

Fig. 3. Change in incidence over time for each category of SES. The change in incidence for two types of gynaecological cancers: endometrial (A) and ovarian (B) cancer for the period before COVID-19 (2017–2019) and during COVID-19 (2020) per month for low, intermediate and high SES. [1]first lockdown 2020, [2]second lockdown 2020.

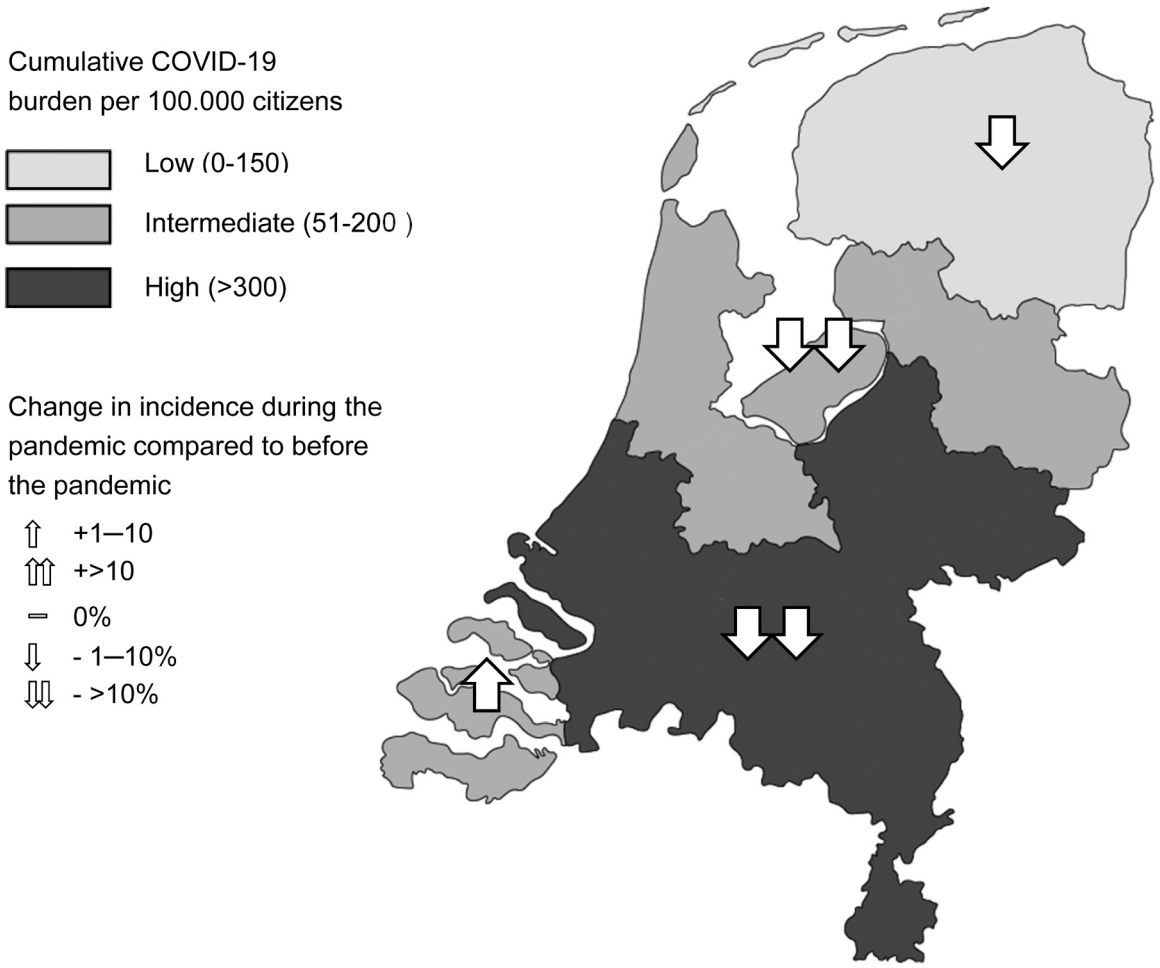

Fig. 4. Change in incidence in the Netherlands during the first wave (March-June) of the COVID-19 pandemic. Map of the Netherlands with the change in incidence for gynaecological cancer during the first wave of COVID-19 (March-June). The colours show the cumulative COVID-19 burden per 100.000 in the period March-June. The arrows indicate an in/decrease in incidence during the pandemic compared to the period before the pandemic.

Furthermore, in person visits to the general practitioner (GP) were partially replaced by telephone or videocall without physical examination [33]. This could have resulted in fewer abnormal findings based on non-specific symptoms which caused a delay in diagnosis. Moreover, in March 2020, there was a temporary halt to the cervical cancer screening programme. Fewer invitations to participate in the cervical cancer screening programme were sent out, which may have resulted in fewer diagnoses of precancerous lesions [34]. Several studies predicted an increase in cervical cancer due to the temporary halt of the screening programme [35,36]. Further research is needed to investigate the exact cause of the drop in incidence, and the increase in incidence in 2021.

Our study showed an increase in incidence in 2021 compared to the period before COVID-19 (2017–2019) and 2020 (5.9 %). The question remains whether the catch-up in delayed diagnosis was completed in 2021, catch-up continued in 2022 or that patients died undiagnosed. A recent report published by the Netherlands Comprehensive Cancer organisation (IKNL) showed the expected incidence of (gynaecological) cancer until 2032 [37]. For both cervical and ovarian cancer a slight decrease in incidence is expected in the next few years, possibly due to the HPV vaccination and the use of contraceptives, while for endometrial cancer an increase in incidence is expected, possibly due to obesity and/or the aging population. Based on the incidences in 2021, the comparison of the mean incidence in 2020 and 2021 with the period before COVID-19 (3.0 % increase in incidence) and the afore mentioned report, we conclude that it is likely that the catch-up of delayed gynaecological cancer diagnosis during COVID-19 (2020) was completed in 2021.

Surprisingly we found no statistically significant difference in incidence between SES groups. This finding was supported by a Turkish study which suggested that the consequences of the COVID-19 pandemic with regard to fear and consequent patient delay impacted all SES groups equally [38]. Although SES can be more variable in Turkey than in the Netherlands, our results suggest that SES by itself may not influence the decrease in number of diagnoses and decrease in incidence.

Given the difference in COVID-19 burden throughout the country, we tried to evaluate the impact of the pandemic on the incidence of gynaecological cancers. We found no statistically significant differences in gynaecological cancer incidence between the different regions according to COVID-19 burden before and during the COVID-19 pandemic. The difference in COVID-19 burden throughout the country does not seem to impact the increase or decrease in incidence gynaecological cancer during the first wave of the pandemic. We conclude that the decrease in incidence seen regardless of the COVID-19 burden are not caused by the COVID-19 infections, but more likely by the nationwide regulations and restrictions as a result of the lockdown.

Our study gives a clear overview on the influence of the COVID-19 pandemic on the incidence of the four most common gynaecological cancer types in the Netherlands. Data from the nationwide NCR database was used of which the vast majority is pathologically confirmed, but also includes a few cases of patients without a pathologically confirmed malignancy, which gives a complete overview of the incidence in the Netherlands. However, this study had some limitations. First, the incidence of gynaecological cancer is relatively low, especially for cervical cancer and vulvar cancer, which hampers robust statistical analyses. Secondly, the use of SES data has a limitation since postal codes are used as a proxy of SES. For this reason SES cannot accurately be estimated in around 11 % of patients. Patients living in a postal code area with fewer than 10 addresses are missing, for reasons of anonymisation of databases. Such areas could either be wealthy villa districts or poorer, sparsely populated areas. Although this method has proven to be useful and reliable, this could have led to an underestimation of certain SES groups, although the difference will be small because of the small number of patients from whom the postal code was missing.

Our results show that the initial wave of the COVID-19 pandemic in the Netherlands had a profound effect on the incidence of gynaecological cancer, on highly symptomatic tumour types as well as of tumour types known from scarcity of symptoms or severe symptoms, but with a high mortality. After the first wave a nearly complete catch up is seen, illustrating good organisation and accessibility of health care. Interestingly no relationship with SES was shown. Future studies will be necessary to evaluate the impact of delayed diagnosis on outcome.

Since the measures taken against COVID-19 seemed to be more important than the burden of the pandemic itself, we advise primary health care should remain easy accessible to prevent delayed diagnosis, especially for cancer types with non-specific symptoms like ovarian cancer.

5. Conclusion

It can be concluded that there was a profound decrease in gynaecological cancer diagnoses during the first wave of the COVID-19 pandemic in 2020 in the Netherlands. This decrease was caught up at the end of 2020 and in 2021, demonstrated by an increase in incidence compared to the reference period (2017–2019). The delay in diagnosis is likely caused by the (nationwide) measures during the pandemic and not by the pandemic itself. All SES groups were equally affected by the pandemic and the lockdown measures, indicating an equality with regard to accessibility of health care. Future studies are needed to investigate how the pandemic impacted the stage at diagnosis, treatment and outcome in order to provide a complete picture of the impact of the COVID-19 pandemic on gynaecological cancer care in the Netherlands.

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CRediT authorship contribution statement

E.J. Oymans: Formal analysis, Writing - Original Draft. **C.D. de Kroon**: Conceptualization, Writing - Review & Editing, Supervision. **J. Bart**: Conceptualization, Writing - Review & Editing, Supervision. **H.W. Nijman**: Writing - Review & Editing. **M.A. van der Aa**: Conceptualization, Writing - Review & Editing, Supervision.

Declaration of Competing Interest

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